UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/823,973	04/14/2004	James J. Gibbons JR.	AM-101323USA	5335

38199 7590 05/17/2007

HOWSON AND HOWSON/WYETH
CATHY A. KODROFF
SUITE 210
501 OFFICE CENTER DRIVE
FT WASHINGTON, PA 19034

EXAMINER	
FETTEROLF, BRANDON J	

ART UNIT	PAPER NUMBER
1642	

MAIL DATE	DELIVERY MODE
05/17/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/823,973	GIBBONS ET AL.	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *2,26 and 28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2, 26 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/07/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/26/2007 has been entered.

Claims 2, 26 and 28 are currently pending and under consideration.

Information Disclosure Statement

The Information Disclosure Statement filed 2/07/2007 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. A signed copy of the IDS is attached hereto.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 26 and 28 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2 and 26 recites "an effective amount" of the claimed synergistic combination. This limitation is indefinite because it is not clear what the amount being administered is effective *for*. The preamble of the claim is not linked to the body of the claim in such a way as to clearly convey that the "effective amount" being administered is effective to treat the condition recited in the preamble. The phrase "an effective amount" has been held to be indefinite when the claim fails to state the function which is to be achieved and more than one effect can be implied from the specification or the relevant art. *In re Fredericksen* 213 F.2d 547, 102 USPQ 35 (CCPA 1954). This rejection may be overcome by amending the claim to recite "a therapeutically effective amount".

For the purposes of examination, the Examiner has interpreted "an effective amount" to mean an amount effective to treat renal cancer as recited in the preamble of the claim.

Claim 28 recites "a synergistic amount" of the claimed combination. This limitation is indefinite because it is not clear what the amount is synergistic *for*. The preamble of the claim is not linked to the body of the claim in such a way as to clearly convey that the "synergistic amount" is effective for. This instant case is amendable to the type of analysis set forth in *In re Fredericksen* 213 F.2d 547, 102 USPQ 35 (CCPA 1954), wherein the phrase "an effective amount" has been held to be indefinite when the claim fails to state the function which is to be achieved and more than one effect can be implied from the specification or the relevant art.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 2, 26 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muss et al. (J. Clinical Oncology 1987; 5: 286-291, of record) in view of Raymond et al. (Proceedings of ASCO 2000; 19: 187a, IDS) and Stebbing et al. (BJU International 2001; 87: 599-601).

Muss et al. teach a method of treating renal cell carcinoma comprising administering a therapeutically effective amount of interferon alpha (Title and page 287, 1st column, *IFN Preparation*

and Study Design). Specifically, the reference teaches a modest but definite antitumor effect of interferon alpha in advanced renal cell carcinoma.

Muss et al. do not explicitly teach the combination of CCI-779 and interferon alpha for the treatment of renal cell carcinoma or a pharmaceutical pack/composition comprising CCI-779 and interferon alpha.

Raymond et al. teach the antitumor effect of the Rapamycin analog, CCI-779. Specifically, the reference teaches a method of treating renal carcinoma and IL-2/IFNα, e.g., intereluekin-2/interferon α resistant renal cell carcinomas comprising administering CCI-779 to a patient (2nd column, abstract 728, 7th line from bottom).

Stebbing et al. teach the current status of interferon-a treatment in advanced renal cancer and conclude that interferon-α at 10 MU subcutaneously three times per week is the standard treatment of renal cancer and should represent the control arm of future studies.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of the references so as to treat renal cell carcinoma because each of the therapeutics had been individually taught in the prior art to be successful at treating renal cell carcinoma. Moreover, in view of the teachings of Stebbing et al., interferon-α treatment in advanced renal cancer is the standard treatment of renal cancer and should represent the control arm of future studies. Thus, the instant situation is amenable to the type of analysis set forth in In re Kerkhoven,205 USPQ 1069 (CCPA 1980) wherein the court held that it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose in order to for a third composition that is to be used for the very same purpose since the idea of combining them flows logically from their having been individually taught in the prior art. Applying the same logic to the instant claims, one of ordinary skill in the art would have reasonable expectation of success that by administering a combination of interferon alpha and CCI-779 to a patient suffering from renal cell carcinoma, one would achieve a method of treating renal cell carcinoma in a patient in need thereof.

Note: In order to expedite prosecution, the Examiner would like to address Applicants arguments pertaining to the previous rejection of claims under 35 U.S.C. 103(a) as being unpatentable over Muss et al. (J. Clinical Oncology 1987; 5: 286-291) in view of Raymond et al.

(Proceedings of ASCO 2000; 19: 187a, IDS) as they relate to the instant rejection. In response to the previous rejection, Applicants assert that even if it could be considered obvious to select interferon alpha and CCI-779 for combination, there can be no expectation that the combination would produce a synergistic effect. In particular, Applicants assert that the unexpected results have been demonstrated because the synergistic effect was observed by administering CCI-779 and IFN-a for the treatment of renal cancer (see, for example, the specification at page 13, lines 19-22). Thus, Applicants assert that the claims explicitly recite this feature.

These arguments have been carefully considered, but are not found persuasive.

Regarding Applicants assertions of unexpected results, the Examiner acknowledges that the specification teaches that the data shown on page 13, Table 1 demonstrates "that CCI-79 and IFN-a are synergistic in this test procedure in that they were able to achieve an effect (tumor regression) not attainable with single agent treatment." However, the Examiner recognizes that the specification appears to be silent on whether these results were "unexpected". Thus, the arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant. *See* MPEP 716.01 (c). In addition, the Examiner recognizes that while the claims recite a "synergistic combination", this recitation does not appear to imply a synergistic "effect" on the inhibition of tumor growth.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2, 26 and 28 are rejected under 35 U.S.C. 103(a) as being obvious over Gibbons et al. (US 2005/0187184, filed 12/06/2001) in view of Stebbing et al. (BJU International 2001; 87: 599-601).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Gibbons et al. teach a method of treating a neoplasm in a mammal comprising alternating administration of CCI-779 and an antimetabolite antineoplastic agent (page 6, Claim 4 of the PG Pub). With regards to the neoplasm, Gibbons et al. teach that the combination is useful for the treatment of renal cancer (paragraph 0010). Moreover, Gibbons et al. teach that the instant combination can be used as part of a chemotherapy cocktail comprising additional antineoplastic agent such as interferons depending on the nature of the neoplasia to be treated (paragraph 0041).

Gibbons et al. do not explicitly teach that the interferon is interferon α.

Stebbing et al. teach the current status of interferon-a treatment in advanced renal cancer and conclude that interferon-α at 10 MU subcutaneously three times per week is the standard treatment of renal cancer and should represent the control arm of future studies.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to include the interferon-alpha in the chemotherapy cocktail as taught by Gibbons et al. for the treatment of renal cancer in view of the teachings of Stebbing et al. One would have been motivated to do so because Stebbing et al. teach that interferon-α treatment in

advanced renal cancer is the standard treatment of renal cancer and should represent the control arm of future studies. Thus, one of ordinary skill in the art would have reasonable expectation of success that by including the interferon-alpha in the chemotherapy cocktail as taught by Gibbons et al. for the treatment of renal cancer in view of the teachings of Stebbing et al., one would achieve a method of treating renal cell carcinoma in a patient in need thereof.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2, 26 and 28 are rejected under 35 U.S.C. 103(a) as being obvious over Dukart et al. (US 2006/0030547, filed 6/1/2006) in view of Stebbing et al. (BJU International 2001; 87: 599-601).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Dukart et al. teach a method of treating a neoplasm in a mammal comprising alternating administration of CCI-779 and an antimetabolite antineoplastic agent (page 5, Claim 1 of the PG

Pub). With regards to the neoplasm, Dukart et al. teach that the combination is useful for the treatment of renal cancer (paragraph 0010). Moreover, Dukart et al. teach that the instant combination can be used as part of a chemotherapy cocktail comprising additional antineoplastic agent such as interferons depending on the nature of the neoplasia to be treated (paragraph 0041).

Gibbons et al. do not explicitly teach that the interferon is interferon α.

Stebbing et al. teach the current status of interferon-a treatment in advanced renal cancer and conclude that interferon-α at 10 MU subcutaneously three times per week is the standard treatment of renal cancer and should represent the control arm of future studies.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to include the interferon-alpha in the chemotherapy cocktail as taught by Gibbons et al. for the treatment of renal cancer in view of the teachings of Stebbing et al. One would have been motivated to do so because Stebbing et al. teach that interferon-α treatment in advanced renal cancer is the standard treatment of renal cancer and should represent the control arm of future studies. Thus, one of ordinary skill in the art would have reasonable expectation of success that by including the interferon-alpha in the chemotherapy cocktail as taught by Gibbons et al. for the treatment of renal cancer in view of the teachings of Stebbing et al., one would achieve a method of treating renal cell carcinoma in a patient in need thereof.

Therefore, No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brandon J Fetterolf, PhD
Patent Examiner
Art Unit 1642

BF